

# MULTI-SCALE MODELING OF THE HIPPOCAMPUS: VALIDATION OF HIGHER-LEVEL NETWORK PHENOMENA VIA BEHAVIORALLY RELEVANT GRID CELL INPUT

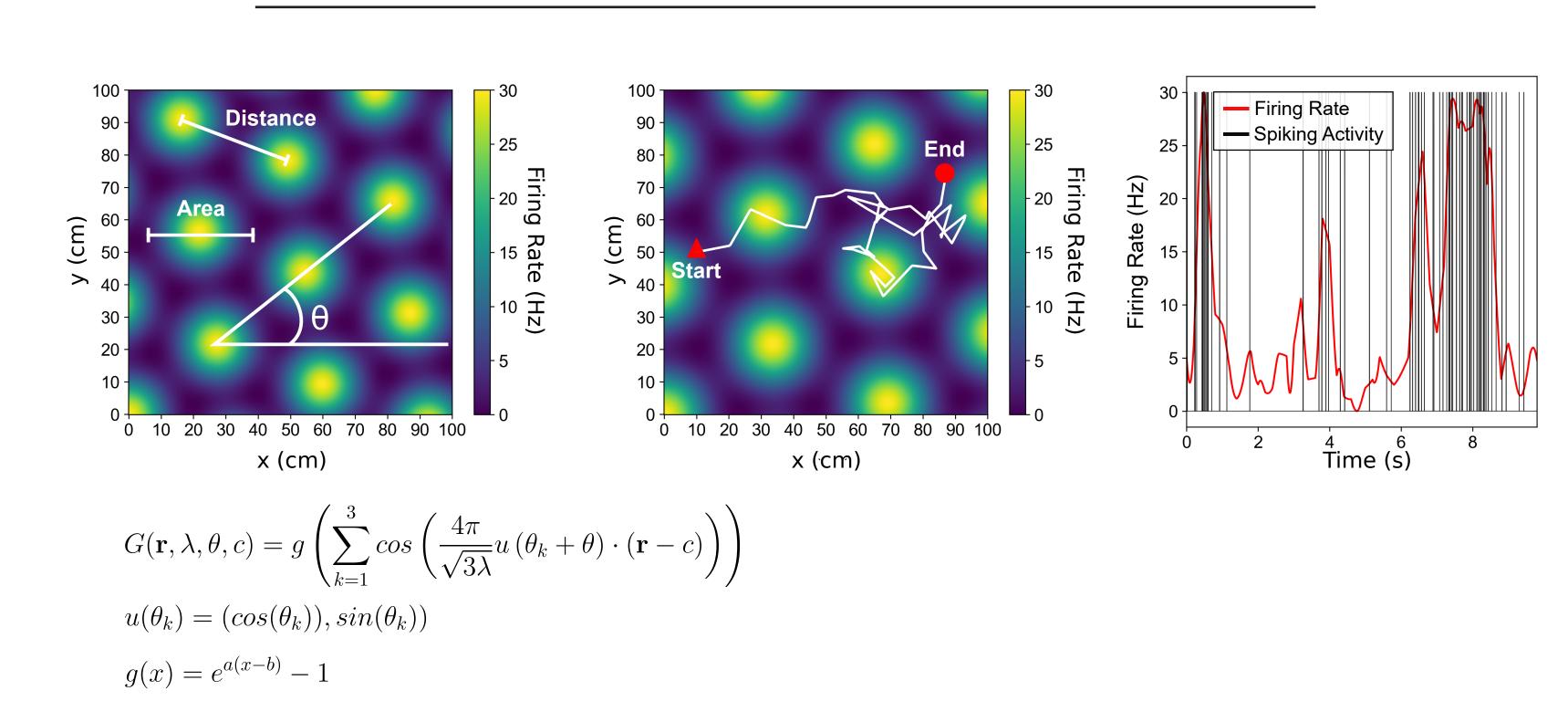
Gene J. Yu, Jean-Marie C. Bouteiller, Dong Song, and Theodore W. Berger

USC Viterbi

#### Summary

- A multi-scale, biologically-realistic neuronal network model of the hippocampus is being developed.
- Physiological input from grid cells as added to the model.
- The model further quantified and integrated two separate studies that revealed that the grid cell receptive field properties and the entorhinal-dentate projection vary along a similar anatomical axis.
- The neuronal network model, with parameters constrained entirely based on experimental data, generated place fields with properties that matched experimental reports and demonstrates a top-down validation strategy that relies on high-level phenomena.
- The model then provided several testable hypotheses and insights:
  - There is a dorso-ventral organization to place field size in dentate gyrus.
  - The entorhinal-dentate topography is necessary to establish this organization.
  - The axon terminal field extent mediates a trade-off between a multi-resolution representation of space and spatial information with both properties optimized at 1.1 mm, which is within the experimentally reported axon terminal field extent of entorhinal cortical axons.

### Physiological Input via Grid Cells<sup>4</sup>

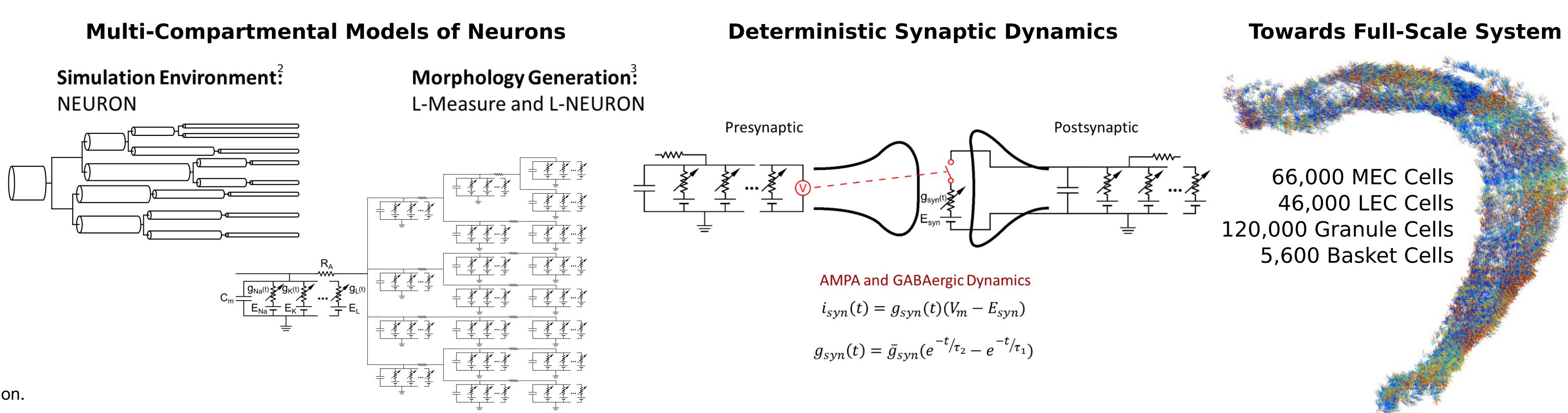


Input firing rates were generated using the grid maps and the location of a virtual rat as it explored a square environment.

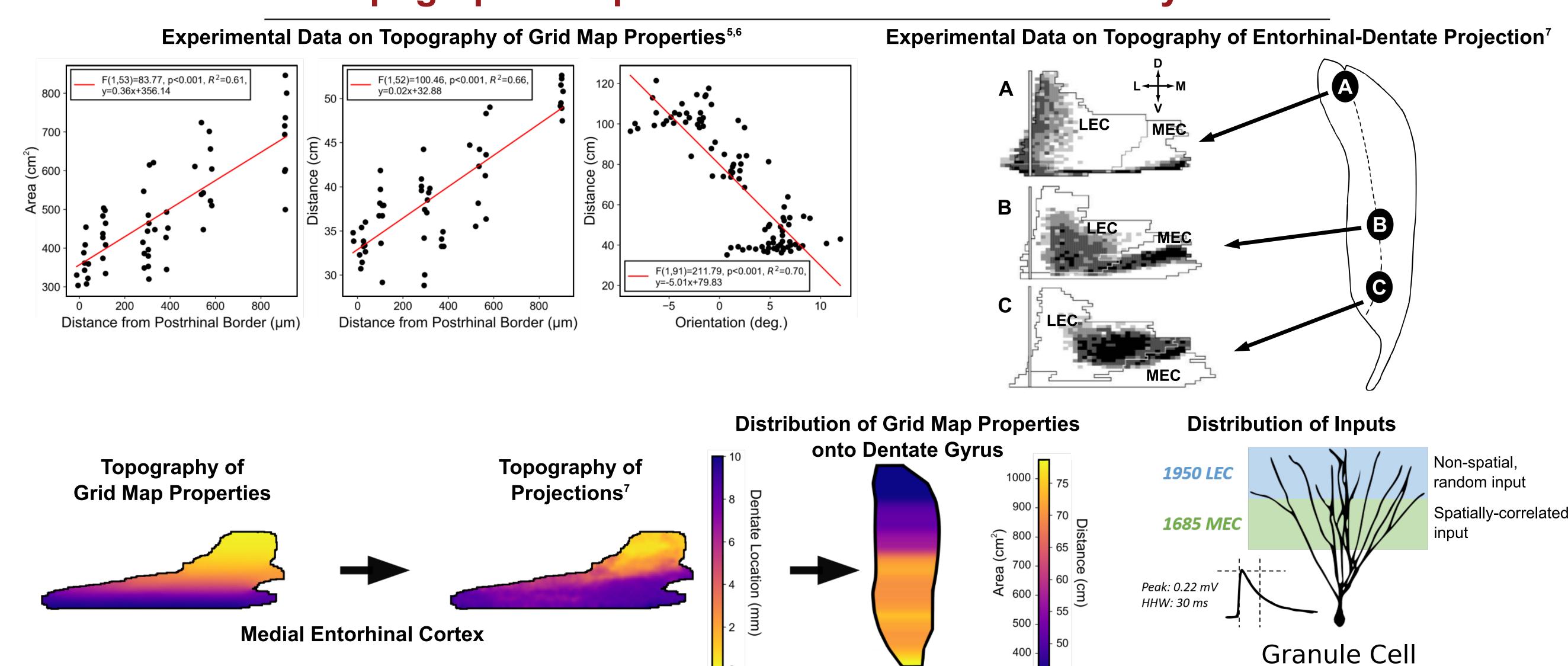
Input spikes were generated using an inhomogeneous Poisson process.

### Large-Scale, Biologically Realistic, Neuronal Network Model of the Hippocampus<sup>1</sup>

Department of Biomedical Engineering, University of Southern California, Los Angeles, USA.

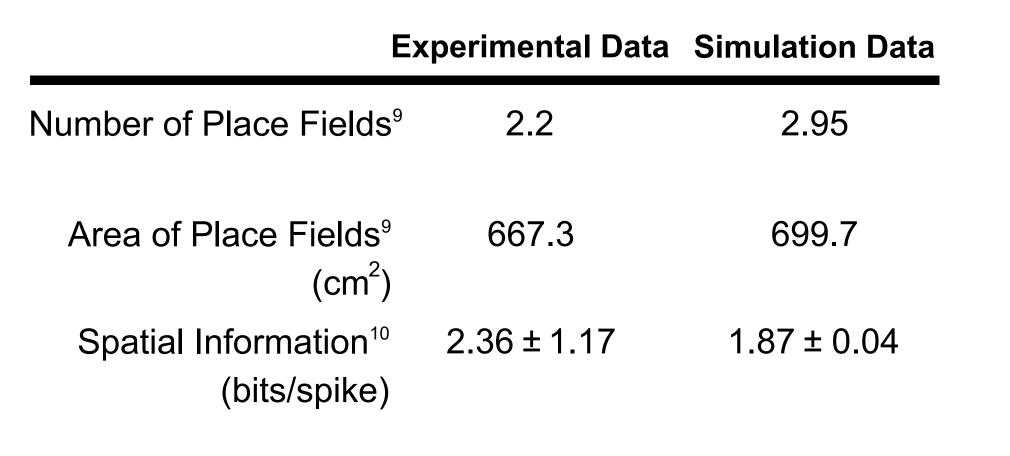


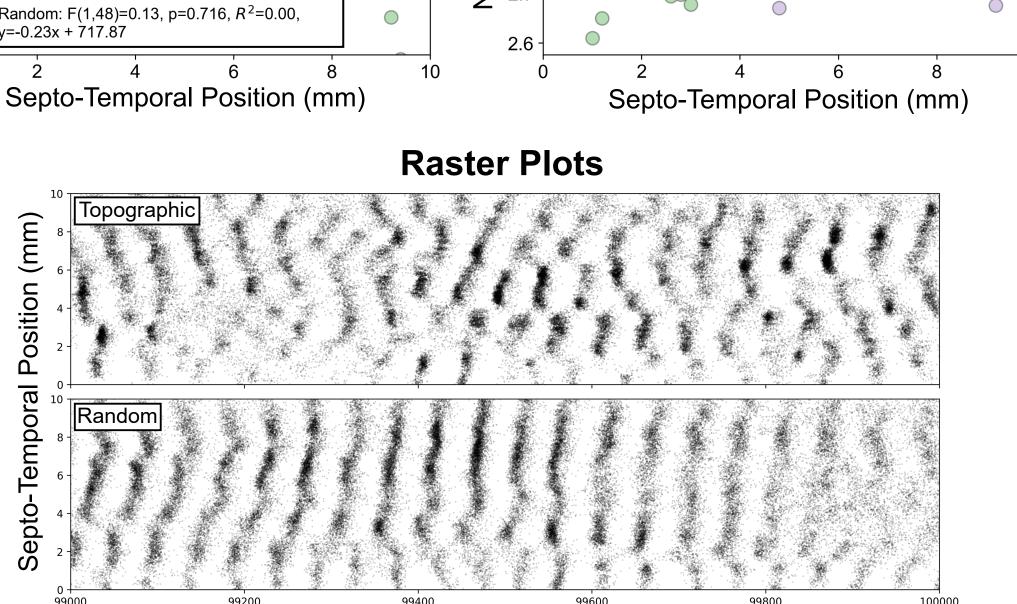
# Topographic Maps Within Entorhinal-Dentate System



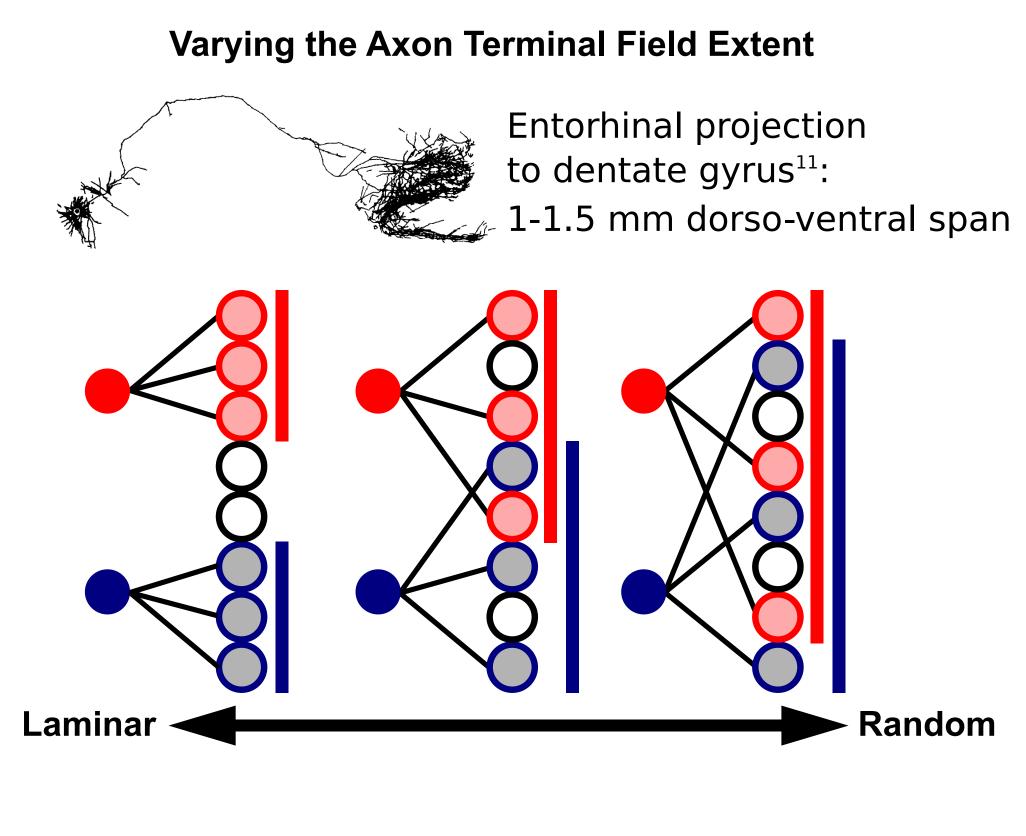
## Validation: Emergence of Place Fields

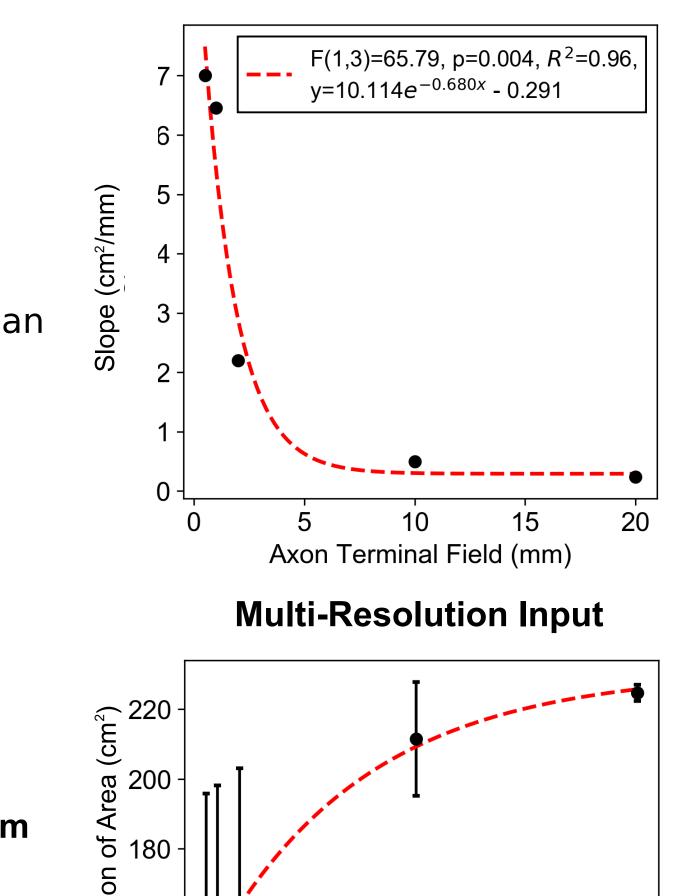
#### **Emergence of Place Field Gradient** Formation of Place Fields<sup>8,9</sup> Simulation Data Experimental Data Topographic: F(1,48)=9.96, p=0.003, R<sup>2</sup>=0.1 Random: F(1,48)=1.07, p=0.306, $R^2=0.02$ , Topographic: F(1,48)=30.13, p<0.001, $R^2=0.39$ , y=-6.45x + 746.42 y = -0.23x + 717.87





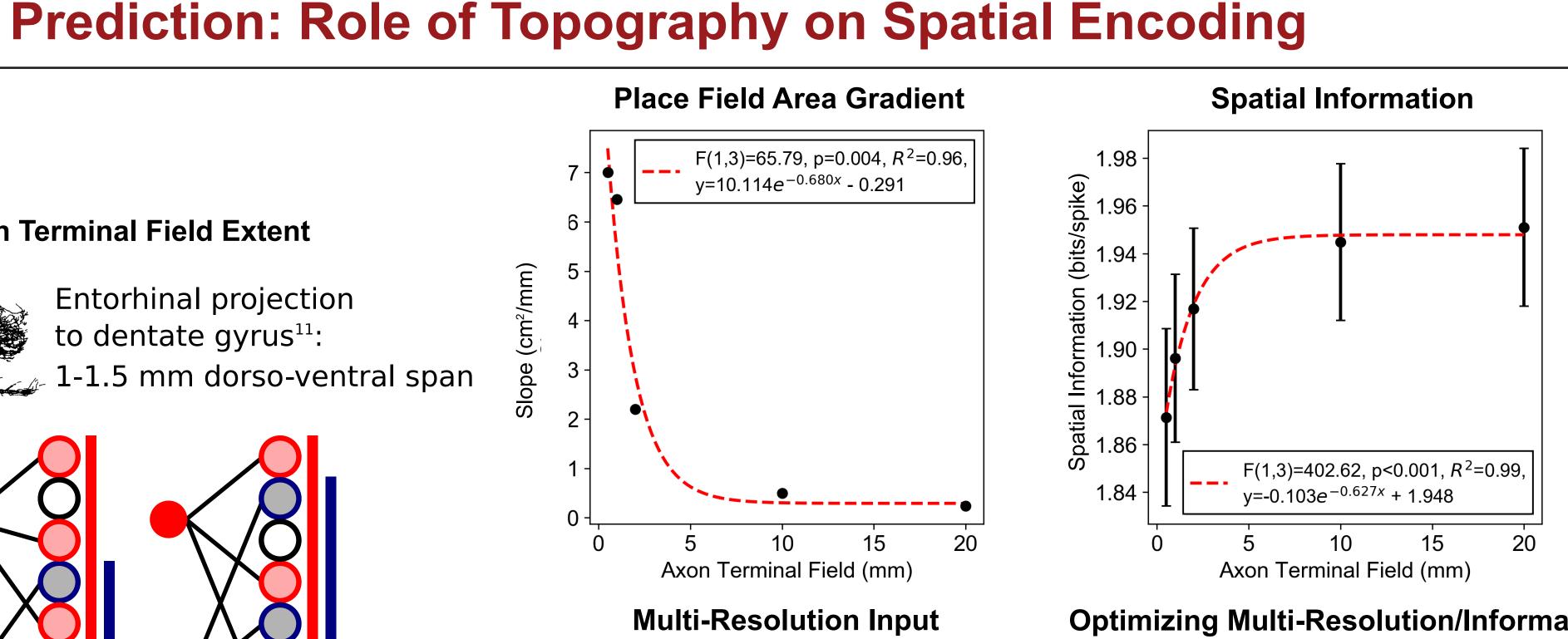
Time (ms)

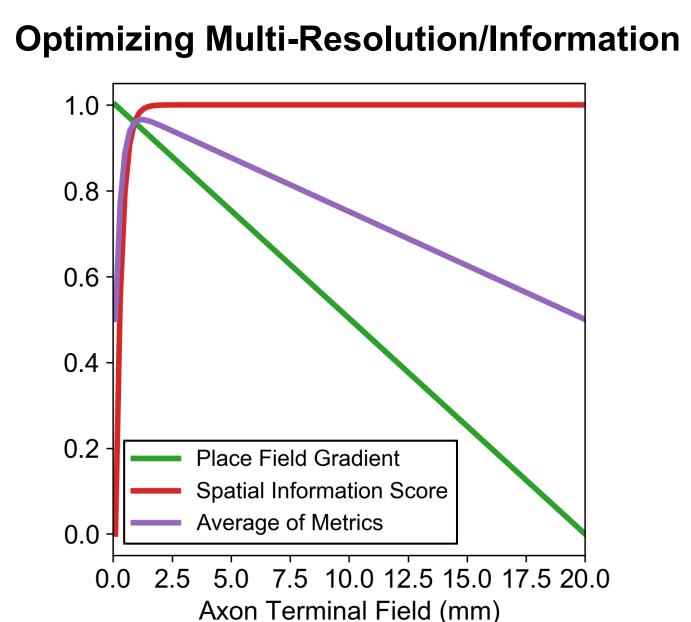




**Dentate Gyrus** 

**Place Field Area Gradient** 





IEEE Trans in Biomed Eng 99:1. 2. Carnevale NT and Hines ML (2006) The NEURON Book. Cambridge, UK: Cambridge University Press 3. Ascoli GA and Krichmar JL (2000). L-neuron: A modeling tool for the efficient generation and parsimonious description of dendritic morphology. Neurocomputing 32-33: 1003-1011.

4. Blair HT, Welday AC, Zhang K (2007) Scale-invariant memory representations emerge from moire interference between grid fields that produce theta oscillations: A computational model. 5. Hafting T, Fyhn M, Molden S, Moser M-B, and Moser E-I (2005). Microstructure of a spatial map in the entorhinal cortex. Nature 436: 801-806.

6. Stensola H, Stensola T, Solstad T, Froland K, Moser M-B, and Moser E-I (2012). The entorhinal grid map is discretized. Nature 492: 72-78 7. Dolorfo CL and Amaral DG (1998) Entorhinal cortex of the rat: Topographic organization of the cells of origin of the perforant path projection to the dentate gyrus. J Comp Neurol 398:25-48. 8. Neunuebel JP and Knierim JJ (2012). Spatial firing correlates of physiologically distinct cell types of the rat dentate gyrus. J Neurosci 32: 3848-3858 9. Leutgeb JK, Leutgeb S, Moser M-B, and Moser E-I (2007). Pattern separation in the dentate gyrus and CA3 of the hippocampus. Science 315: 961-966. 10. Jung MW and McNaughton BL (1993). Spatial selectivity of unit activity in the hippocampal granular layer. Hippocampus 3: 165-182. 11. Tamamaki N and Nojyo Y (1993). Projection of the entorhinal layer II neurons in the rat as revealed by intracellular pressure-injection of neurobiotin. Hippocampus 3: 471-480. Computation was supported by the USC Center for High-Performance Computing and Communications (www.usc.edu/hpc).

F(1,3)=655.50, p<0.001,  $R^2=0.995$ 

 $v = -89.442e^{-0.142x} + 230.954$ 

Axon Terminal Field (mm)